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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/772,374	02/06/2004	Benjamin Gaston	28195-503 CON	6783

20306 7590 08/01/2005

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EXAMINER	
HENLEY III, RAYMOND J	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 08/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/772,374	GASTON ET AL.	
	Examiner	Art Unit	
	Raymond J. Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 9* is/are rejected.

7)☒ Claim(s) *9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Declaration under 37 C.F.R. 1.132.

CLAIMS 1 AND 9 ARE PRESENTED FOR EXAMINATION

Applicants' amendment filed July 15, 2005 has been received and entered into the application. Accordingly, claim 9 has been amended.

In view of the above amendment, the rejection of claim 9 under 35 U.S.C. § 112, first paragraph, as set forth in the previous Office action dated April 12, 2005 is withdrawn.

The indicated allowability of claim 1 is withdrawn in view of the newly discovered reference relied on below. The reference was discovered during an search update in various data bases. The Examiner regrets the delay in this matter.

Specification

Upon review of Applicants' amendment to the specification filed January 10, 2005, it is noted that the filing date of the parent application is erroneously set forth as October 15, 2001. Therefore, in the present specification at page 1, as amended, "10/380,763 filed October 15, 2001" should be changed to ---10/380,763 filed March 24, 2003---.

Claim Objection

Upon further consideration of claim 9, it is objected to for the following reasons.

For the sake of clarity, the term "CF" in the expression "in the CF airway" (line 4) should be re-written as ---in the airway of said patient---. This would remove any possible confusion as to the meaning of the expression "CF airway", while clearly setting forth a concept that is implicitly supported in the specification as originally filed, i.e., the airway of a patient suffering from cystic fibrosis.

Also, because of the current construction of claim 9, the limiting effect of the expression "as acute therapy" is unclear.

It is suggested that ", or an amount to ameliorate bronchoconstriction...as acute therapy,", (claim 9, lines 4-6) be amended to read ---or an amount, given acutely, to ameliorate an exacerbation of bronchoconstriction, mucus plugging and/or bacterial bronchitis/bronchiolitis, where the composition...complex.".

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 9 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 14 and 15 of U.S. Patent No. 6,627,602. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

Patented claim 1 is directed to a method for treating a patient with a disease or pathologic condition associated with G-protein receptor kinase activity which comprises the administration of a nitric oxide donor. Patented claim 2 provides for the nitric oxide donor being an S-

nitrosothiol, i.e., S-nitrosoglutathione. Patented claim 15 provides for the disease or pathologic condition being cystic fibrosis. Also, the nitric oxide donor of the patented method may be ethyl nitrite (see the specification of the '602 patent at col. 3, line 39). It is believed that the Examiner's reliance on the specification of the '602 patent is proper. "The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. *In re Boylan*, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In re Vogel, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970)", (MPEP § 804).

While the patented claims do not include the limitations that the nitric oxide donor is administered as an aerosol and administered to the nasal mucosa and osteomeatal complex, the present claims would serve as an anticipatory reference against the patented claims. The recited functions of the patented claims, e.g., that the nitric oxide donor "provides bioactivity that is identified with nitric oxide to inhibit G-protein receptor kinase activity thereby sensitizing or preventing desensitization of said receptor" (patented claim 1), are presumed to be inherent in the method of the present claims because the same active agents are administered to the same host. Accordingly, a conclusion of obviousness is proper.

It is noted that patented claim 14 requires that when the disease is cystic fibrosis, the nitric oxide donor is administered in an amount which is insufficient to acutely lower FEV1 by more than 12%. While the Examiner cannot determine if the amounts administered in the present claims would encompass such amounts, ("As a practical matter, the Patent Office is not

equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972), see MPEP § 2113, last sentence), the amounts of the patented claims and those of the present claims would appear to at least overlap because in both sets of claims, the amount of the active agent that is administered is nevertheless effective for the ultimate purpose of treating cystic fibrosis.

Accordingly, for the above reasons, the claims are deemed properly rejected.

Comments Concerning the Prosecution of the Parent Application

The following comments are made in order to make the present record as complete as reasonably possible, (see MPEP § 1302.14). In particular, it is believed that the file history of the present application is not reasonably complete with respect to the issue of obviousness under 35 U.S.C. § 103 over, *inter alia*, Garvey et al. (U.S. Patent No. 6,331,543), which issue was raised in the parent application, i.e., Serial No. 10/380,763, ("the '763 application"), (see the Office action dated August 21, 2003 in the '763 application), and which was not raised during the prosecution of the present application.

The Examiner did not raise the above issue of obviousness in the present application because of the reasons presented during the prosecution of the parent application. Upon further consideration, the Examiner believes that the following comments should also be of record in the present application as well.

Claim 1 of the present application is representative of the subject matter claimed by Applicants and reads:

> 1. (Previously presented) A method for treating cystic fibrosis, said method comprising the step of administering a therapeutically effective amount of a composition comprising an S-nitrosothiol to a patient having cystic fibrosis, wherein the composition is formulated as a powder or an aerosol and administered to the nasal mucosa and osteomeatal complex.

The other pending claim, claim 9, is substantially the same as claim 1, but requires the administration of ethyl nitrate, which is not an S-nitrosothiol compound as in present claim 1.

Garvey et al., (U.S. Patent No. 6,331,543), is directed to the use of certain nitrosated and/or nitrosylated phosphodiesterase inhibitors, (not compounds of the present invention), and optionally one or more compounds that donate, transfer or release nitric oxide (which would encompass the compounds of the present invention), (see, for example, the abstract). Garvey et al. teaches that the above inhibitors and compounds may be used for treating diseases induced by the increased metabolism of cyclic guanosine 3', 5'-monophosphate (cGMP). The treatment of cystic fibrosis is disclosed as such a disease (see col. 4, line 67). S-nitrosothiols are also disclosed (col. 53, line 62 – col. 54, line 67). Garvey et al. also teach that the compositions may be administered by inhalation spray (col. 58, lines 17-20).

One of ordinary skill in the art would apparently not have had a reasonably expectation of success in treating cystic fibrosis as disclosed, but not claimed, by Garvey et al. because in a declaration under 37 C.F.R. § 1.132 filed September 23, 2003 in the '763 application, (a copy of which is attached hereto) it was averred that cystic fibrosis, or the symptoms thereof, were not associated with cGMP. The Examiner accepts such statement.

Also, even if a reasonable expectation of success for treating cystic fibrosis was present in Garvey et al., the Examiner believes that one of ordinary skill in the art would not have been

motivated to administer the active agents of Garvey et al. in the manner presently claimed, i.e., "administered to the nasal mucosa and oseomeatal complex", because the symptoms of cystic fibrosis include respiratory conditions, such as accumulation of mucus in the cystic fibrosis airway (see present claim 9), For a patient suffering from pulmonary conditions such as bronchoconstriction, mucus plugging, (i.e., in the lungs), and/or bacterial bronchitis/bronchiolitis (see present claim 9), it is believed that one of ordinary skill in the art reading the teaching of Garvey et al. to administer the compounds by inhalation spray, would have been motivated to administer such compounds to the site of pathology, i.e., the lungs, rather than to the nasal mucosa and osteomeatal complex.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J. Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Raymond J Henley III
Primary Examiner
Art Unit 1614

July 28, 2005

ATTACHMENT TO
OFFICE ACTION

#6

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

03 SEP 23 P1:17

In re Application of	)	
	)	
BENJAMIN GASTON, et al.	)	Group Art Unit: 1614
	)	
Patent Application No. 10/380,763	)	Examiner: R.J. Hendley III
	)	
Filed: March 24, 2003	)	
	)	
For: THERAPEUTIC USE OF AEROSOLIZED S-NITROSOGLUTATHIONE IN CYSTIC FIBROSIS	)	

DECLARATION UNDER 37 C.F.R. 1.132

Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

JONATHAN S. STAMLER and BENJAMIN GASTON hereby declare:

1. We are the inventors in the above-identified patent application.

2. Benjamin Gaston has an M.D. degree and is an Associate Professor of Pediatrics at the University of Virginia (Charlottesville). He trained at Brigham Women's Hospital (Harvard Medical School). He is a practicing pulmonologist. He is an expert in cystic fibrosis and pulmonary medicine.

3. Dr. Gaston is involved in an ongoing clinical investigation where aerosolized S-nitrosoglutathione in administered to patients with cystic fibrosis.

4. Jonathan Stamler has an M.D. degree and is a Professor of Medicine and Biochemistry at Duke University. He is also an Associate Investigator of the Howard Hughes Medical Institute at the Duke University Medical Center in Durham, North Carolina. He is a practicing cardiologist

and pulmonologist. He is co-author of a book titled "Methods in Nitric Oxide Research", John Wiley & Sons, New York, 1996.

5. Cystic fibrosis is not associated with vasoconstriction or constriction of corpus cavernosum.

6. Cystic fibrosis is not known to be induced by the increased metabolism of cGMP.

7. Increased levels of cGMP are not known to be beneficial for amelioration of cystic fibrosis symptoms.

8. Endogenous levels of EDRF relate to vascular function and not to symptoms of cystic fibrosis.

9. We are familiar with Garvey et al U.S. Patent No. 6,331,541 B1. Garvey et al administers phosphodiesterase inhibitor to block the breakdown of cGMP. Garvey et al administers NO donor to increase the amount of cGMP present by reacting NO with heme of guanylate cyclase. The point in Garvey et al is to provide an increased level of cGMP to relax blood vessels or corpus cavernosum.

10. In view of the point in Garvey et al being to increase level of cGMP and in view of cystic fibrosis not being induced by the increased metabolism of cGMP or having symptoms related to endogenous levels of EDRF, one skilled in the art would not believe Garvey's method would be beneficial in the treatment of cystic fibrosis even though Garvey lists cystic fibrosis as one of the disorders induced by metabolism of cGMP.

11. We further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are

punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date

Benjamin Gaston

9/9/03
Date

Jonathan S. Stamler

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

BENJAMIN GASTON, et al.

Patent Application No. 10/380,763

Filed: March 24, 2003

For: THERAPEUTIC USE OF AEROSOLIZED S-NITROSOGLUTATHIONE IN CYSTIC FIBROSIS

Group Art Unit: 1614

Examiner: R.J. Hendley III

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11 Sept 03
Date

Benjamin Gaston

Date

Jonathan S. Stamler